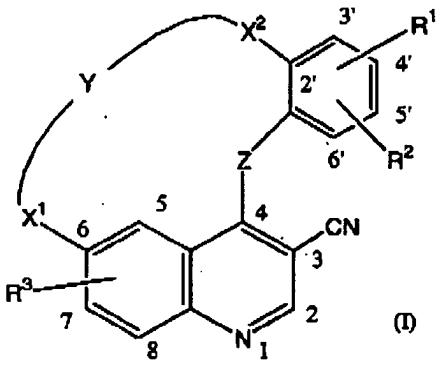
Listing of Claims

This listing of claims replaces all prior versions, and listings, of claims in the captioned application.

1. (currently amended) A compound having the formula



(I)

the *N*-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein

Z represents ~~O,~~ NH ~~or S~~;

Y represents ~~C_{3-9}alkyl , C_{3-9}alkenyl , C_{1-5}alkyl-oxy-C_{1-5}alkyl ,~~
$-C_{1-5}$alkyl-NR^{12}-C_{1-5}alkyl~~-, C_{1-5}alkyl-NR^{13}-CO-C_{1-5}alkyl ,~~
~~C_{1-5}alkyl-CO-NR^{14}-C_{1-5}alkyl , C_{1-6}alkyl-CO-NH , C_{1-6}alkyl-NH-CO ,~~
~~CO-NH-C_{1-6}alkyl , NH-CO-C_{1-6}alkyl , CO-C_{1-7}alkyl , C_{1-7}alkyl-CO ,~~
~~C_{1-6}alkyl-CO-C_{1-6}alkyl, C_{1-2}alkyl-NH-CO-CH_2R^{15}-NH~~ ;

X^1 represents ~~a direct bond, O, O-C_{1-2}alkyl , CO, CO-C_{1-2}alkyl , NR^{10},~~
~~NR^{10}-C_{1-2}alkyl , NR^{16}-CO , NR^{16}-CO-C_{1-2}alkyl, O-N=CH- or C_{1-2}alkyl;~~

~~X^2 represents a direct bond, O, O-C_{1-2}alkyl , CO, CO-C_{1-2}alkyl , NR^{11},~~
~~NR^{11}-C_{1-2}alkyl , NR^{17}-CO , NR^{17}-CO-C_{1-2}alkyl, Het^{20}-C_{1-2}alkyl, O-N=CH- or C_{1-2}alkyl~~;

R^1 represents hydrogen, cyano, halo, hydroxy, formyl, C_{1-6}alkoxy-, C_{1-6}alkyl-,
C_{1-6}alkoxy- substituted with halo,
C_{1-4}alkyl substituted with one or where possible two or more substituents selected from hydroxy or halo;

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R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, Het^{16}-carbonyl-, C_{1-4}alkyloxycarbonyl-, C_{1-4}alkylcarbonyl-, aminocarbonyl-, mono-or di(C_{1-4}alkyl)aminocarbonyl-, Het^1, formyl, C_{1-4}alkyl-, C_{2-6}alkynyl-, C_{3-6}cycloalkyl-, C_{3-6}cycloalkyloxy-, C_{1-6}alkoxy-, Ar^5, Ar^1-oxy-, dihydroxyborane , C_{1-6}alkoxy- substituted with halo, C_{1-4}alkyl substituted with one or where possible two or more substituents selected from halo, hydroxy or NR^4R^5, C_{1-4}alkylcarbonyl- wherein said C_{1-4}alkyl is optionally substituted with one or where possible two or more substituents selected from hydroxy or C_{1-4}alkyl-oxy-;

R^3 represents hydrogen, hydroxy, Ar^3-oxy, Ar^4-C_{1-4}alkyloxy-, C_{1-4}alkyloxy-, C_{2-4}alkenyloxy- optionally substituted with Het^{12} or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy-, hydroxy, halo, Het^2-, $-NR^6R^7$, -carbonyl- NR^8R^9 or Het^3-carbonyl-;

R^4 and R^5 are each independently selected from hydrogen or C_{1-4}alkyl;

R^6 and R^7 are each independently selected from hydrogen, C_{1-4}alkyl, Het^8, aminosulfonyl-, mono- or di (C_{1-4}alkyl)-aminosulfonyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxycarbonyl-C_{1-4}alkyl-, C_{3-6}cycloalkyl, Het^9-carbonyl-C_{1-4}alkyl-, Het^{10}-carbonyl-, polyhydroxy-C_{1-4}alkyl-, Het^{11}-C_{1-4}alkyl- or Ar^2-C_{1-4}alkyl-;

R^8 and R^9 are each independently selected from hydrogen, C_{1-4}alkyl, C_{3-6}cycloalkyl, Het^4, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or polyhydroxy-C_{1-4}alkyl-;

~~R^{10} represents hydrogen, C_{1-4}alkyl, Het^5, Het^6-C_{1-4}alkyl-, C_{2-4}alkenylcarbonyl- optionally substituted with Het^7-C_{1-4}alkylaminocarbonyl-, C_{2-4}alkenylsulfonyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;~~

~~R^{11} represents hydrogen, C_{1-4}alkyl, C_{1-4}alkyl-oxy-carbonyl-, Het^{17}, Het^{18}-C_{1-4}alkyl-, C_{2-4}alkenylcarbonyl- optionally substituted with Het^{19}-C_{1-4}alkylaminocarbonyl-, C_{2-4}alkenylsulfonyl-, C_{1-4}alkyloxyC_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;~~

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R^{12} represents hydrogen, C_{1-4}alkyl, Het^{13}, Het^{14}-C_{1-4}alkyl- or phenyl optionally substituted with one or where possible two or more substituents selected from hydrogen, hydroxy, amino or C_{1-4}alkyloxy-;

~~R^{13} and R^{14} are each independently selected from hydrogen, C_{1-4}alkyl, Het^{15}-C_{1-4}alkyl- or C_{1-4}alkyloxyC_{1-4}alkyl-;~~

~~R^{15} represents hydrogen or C_{1-4}alkyl optionally substituted with phenyl, indolyl, methylsulfide, hydroxy, thiol, hydroxyphenyl, aminocarbonyl, hydroxycarbonyl, amine, imidazoyl or guanidino;~~

~~R^{16} and R^{17} are each independently selected from hydrogen, C_{1-4}alkyl, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyloxyC_{1-4}alkyl;~~

Het^1 represents a heterocycle selected from piperidinyl, morpholinyl, piperazinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^1 is optionally substituted amino, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl-, phenyl, phenyl-C_{1-4}alkyl-,
C_{1-4}alkyl-oxy-C_{1-4}alkyl- mono- or di(C_{1-4}alkyl)amino- or amino-carbonyl-;

Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino-,
mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-, aminoC_{1-4}alkyl-,
mono- or di(C_{1-4}alkyl)amino-sulfonyl-, aminosulfonyl-;

Het^3, Het^4 and Het^8 each independently represent a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, furanyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^3, Het^4 or Het^8 is optionally substituted with one or where possible two or more substituents selected from hydroxy-, amino-, C_{1-4}alkyl-,
C_{3-6}cycloalkyl-C_{1-4}alkyl-, aminosulfonyl-, mono- or di(C_{1-4}alkyl)aminosulfonyl or amino-C_{1-4}alkyl-;

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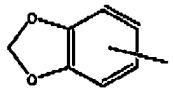
~~Het^5 represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^5 optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;~~

~~Het^6 and Het^7 each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^6 and Het^7 are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;~~

Het^9 and Het^{10} each independently represent a heterocycle selected from furanyl, piperidinyl, morpholinyl, piperazinyl, pyrazolyl, dioxolanyl, thiazolyl, oxazolyl, imidazolyl, isoxazolyl, oxadiazolyl, pyridinyl or pyrrolidinyl wherein said Het^9 or Het^{10} is optionally substituted C_{1-4}alkyl, C_{3-6}cycloalkyl-C_{1-4}alkyl- or amino-C_{1-4}alkyl-;

Het^{11} represents a heterocycle selected from indolyl or  ;

Het^{12} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, thiomorpholinyl or dithianyl wherein said Het^{12} is optionally substituted with one or where possible two or more substituents selected from hydroxy, halo, amino, C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl-, hydroxy-C_{1-4}alkyl-oxy-C_{1-4}alkyl-, mono- or di(C_{1-4}alkyl)amino- or mono- or di(C_{1-4}alkyl)amino-C_{1-4}alkyl-;

Het^{13} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{13} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

Het^{14} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^{14} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy-C_{1-4}allkyl-, C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy-C_{1-4}alkyl-;

~~Het^{15} and Het^{21} each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said heterocycles are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl,~~

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~~hydroxy C_{1-4}alkyl-,~~

~~C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy C_{1-4}alkyl ;~~

Het^{16} represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl, 1,3,2-dioxaborolane or piperidinyl wherein said heterocycle is optionally substituted with one or more substituents selected from C_{1-4}alkyl; and

~~Het^{17} represent a heterocycle selected from pyrrolidinyl or piperidinyl wherein said Het^{17} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy C_{1-4}alkyl , C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy C_{1-4}alkyl ;~~

~~Het^{18} and Het^{19} each independently represent a heterocycle selected from morpholinyl, pyrrolidinyl, piperazinyl or piperidinyl wherein said Het^{18} and Het^{19} are optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy C_{1-4}alkyl , C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy C_{1-4}alkyl ;~~

~~Het^{20} represents a heterocycle selected from pyrrolidinyl, 2 pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, imidazolyl or pyrazolidinyl wherein said Het^{20} is optionally substituted with one or where possible two or more substituents selected from C_{1-4}alkyl, C_{3-6}cycloalkyl, hydroxy C_{1-4}alkyl , C_{1-4}alkyloxyC_{1-4}alkyl or polyhydroxy C_{1-4}alkyl ; and~~

Ar^1, Ar^2, Ar^3, Ar^4 and Ar^5 each independently represent phenyl optionally substituted with cyano, C_{1-4}alkylsulfonyl-, C_{1-4}alkylsulfonylamino-, aminosulfonylamino-, hydroxy-C_{1-4}alkyl, aminosulfonyl-, hydroxy-, C_{1-4}alkyloxy- or C_{1-4}alkyl.

2. (Currently Amended) A compound according to claim 1 wherein;

~~Z represents NH;~~

~~Y represents C_{3-9}alkyl , C_{2-9}alkenyl , C_{1-5}alkyl-oxy-C_{1-5}alkyl , C_{1-5}alkyl-NR^{12}-C_{1-5}alkyl , C_{1-5}alkyl-NR^{13}-CO-C_{1-5}alkyl , C_{1-6}alkyl-NH-CO , CO-C_{1-7}alkyl , C_{1-7}alkyl-CO- or C_{1-6}alkyl-CO-C_{1-6}alkyl;~~

~~X^1 represents O, -O-C_{1-2}alkyl , O-N=CH , NR^{16}-CO, NR^{16}-CO-C_{1-2}alkyl , NR^{10}- or -NR^{10}-C_{1-2}alkyl ; in a particular embodiment X^1 represents -O , -O-CH_2 , NR^{10}- or -NR^{10}-C_{1-2}alkyl ;~~

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~~X^2 represents a direct bond, O, O C_{1-2}alkyl, O N=CH, Het^{20}-C_{1-2}alkyl, C_{1-2}alkyl, NR^{17}-CO, NR^{17}-CO C_{1-2}alkyl, NR^{11} or NR^{11}-C_{1-2}alkyl; in a particular embodiment X^2 represents a direct bond, O N=CH, NR^{11}-C_{1-2}alkyl, NR^{11}-CH_2, Het^{20}-C_{1-2}alkyl, NR^{17}-CO, NR^{17}-CO C_{1-2}alkyl-C_{1-2}alkyl, O C_{1-2}alkyl, O or O CH_2;~~

R^1 ~~represents hydrogen, cyano, halo or hydroxy, preferably~~ halo;

R^2 represents hydrogen, cyano, halo, hydroxy, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl-, C_{2-6}alkynyl-, Ar^5 or Het^1;

In a further embodiment R^2 represents hydrogen, cyano, halo, hydroxy, C_{2-6}alkynyl- or Het^1;

R^3 represents hydrogen, hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;

~~R^{10} represents hydrogen, C_{1-4}alkyl or C_{1-4}alkyl-oxy-carbonyl;~~

~~R^{11} represents hydrogen, C_{1-4}alkyl or C_{1-4}alkyl-oxy-carbonyl;~~

R^{12} represents Het^{14}-C_{1-4}alkyl, in particular morpholinyl-C_{1-4}alkyl;

~~R^{16} represents hydrogen, C_{1-4}alkyl, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyl-oxy-C_{1-4}alkyl; in particular R^{16} represents hydrogen or C_{1-4}alkyl;~~

~~R^{17} represents hydrogen, C_{1-4}alkyl, Het^{21}-C_{1-4}alkyl or C_{1-4}alkyl-oxy-C_{1-4}alkyl; in particular R^{16} represents hydrogen or C_{1-4}alkyl;~~

Het^1 represents thiazolyl optionally substituted amino, C_{1-4}alkyl, hydroxy-C_{1-4}alkyl-, phenyl, phenyl-C_{1-4}alkyl-, C_{1-4}alkyl-oxy-C_{1-4}alkyl- mono- or di(C_{1-4}alkyl)amino- or amino-carbonyl;

Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;

Het^{14} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^{14} is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;

Het^{16} represents a heterocycle selected from piperidinyl, morpholinyl or pyrrolidinyl;

~~Het^{20} represents a heterocycle selected from pyrrolidinyl, 2-pyrrolidinyl or piperidinyl;~~

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~~Het^{21} represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^{21} is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl ;~~

Ar^4 represents phenyl optionally substituted with cyano, hydroxy-, C_{1-4}alkyloxy or C_{1-4}alkyl; and

Ar^5 represents phenyl optionally substituted with cyano, hydroxy, C_{1-4}alkyloxy or C_{1-4}alkyl.

3. (Currently Amended) A compound according to claim 1 wherein;

~~Z represents NH;~~

~~Y represents C_{3-9}alkyl , C_{1-5}alkyl NR^{12} C_{1-5}alkyl , C_{1-5}alkyl NR^{13} CO C_{1-5}alkyl , C_{1-6}alkyl NH CO or CO NH C_{1-6}alkyl ;~~

~~X^1 represents a direct bond, NR^{10}, NR^{10} C_{1-2}alkyl , NR^{10} CH_2 , C_{1-2}alkyl , O C_{1-2}alkyl, O or O CH_2 ;~~

~~X^2 represents a O , NR^{11}, NR^{17} CO, NR^{17} CO C_{1-2}alkyl or Het^{20} C_{1-2}alkyl;~~

R^1 represents hydrogen or halo;

R^2 represents hydrogen, cyano, halo, hydroxycarbonyl-, C_{1-4}alkyloxycarbonyl-, Het^{16}-carbonyl- or Ar^5;

R^3 represents hydrogen, hydroxy, C_{1-4}alkyloxy-, Ar^4-C_{1-4}alkyloxy or R^3 represents C_{1-4}alkyloxy substituted with one or where possible two or more substituents selected from C_{1-4}alkyloxy- or Het^2-;

~~R^{10} represents hydrogen;~~

~~R^{11} represents hydrogen, C_{1-4}alkyl or C_{1-4}alkyl oxy carbonyl ;~~

~~R^{12} represents Het^{14} C_{1-4}alkyl, in particular morpholinyl C_{1-4}alkyl;~~

~~R^{13} represents hydrogen;~~

~~R^{17} represents hydrogen;~~

Het^2 represents a heterocycle selected from morpholinyl, piperazinyl, piperidinyl or pyrrolidinyl wherein said Het^2 is optionally substituted with one or where possible two or more substituents selected from hydroxy, amino or C_{1-4}alkyl-;

Het^{14} represents morpholinyl;

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Het^{16} represents a heterocycle selected from morpholinyl or pyrrolidinyl;

~~Het^{20} represents pyrrolidinyl or piperidinyl;~~

Ar^4 represents phenyl; and

Ar^5 represents phenyl optionally substituted with cyano.

4. (previously presented) A compound according to claim 1, wherein the R^1 substituent is at position 4', the R^2 substituent is at position 5' and the R^3 substituent at position 7 of the structure of formula (I).

5.-7. (Cancelled)

8. (previously presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, an effective kinase inhibitory amount of a compound as described in claim 1.

9.-12 (cancelled)

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